



## HUNTINGTON'S DISEASE LIKE EMERGENCY RESPONDERS AT AN ACCIDENT SCENE, MESENCHYMAL STEM CELLS

move from brain cell to brain cell, looking for the injured. • Jan Nolta, Ph.D., director of the University of California, Davis Institute for Regenerative Cures, intends to harness the paramedic services of these bone marrow-derived cells and treat Huntington's disease. "They are very social," she says of the cells. "They seem to query other cells and ask them if they need anything." Inserted into the brain, they actually seek out damage. • Some 2,000 people are diagnosed with Huntington's every year in the United States. Unlike many inherited diseases, which require two copies of a disease-

causing gene to wreak havoc, Huntington's rears its head with a single mutant gene. That means children of someone with Huntington's have a 50-50 chance of developing the always-fatal disease.

The errant Huntington's gene is a copy machine run amok, repeating the recipe for the same three nucleic acids 38 times or more. The protein created by this wild repetition, called huntingtin or htt, damages a class of brain cells called medium spiny neurons.

When a medium spiny neuron is healthy, it is shaped something like a spider web, with axons extending in all directions, controlling movement, cognition and emotion. But under htt's influence, it pulls in those axons. Cell-to-cell communication stops, and the person develops involuntary dance-like movements. The condition leads to behavior changes; a sweet-tempered person becomes irascible. Cognitive function declines.

To disrupt this destruction, Nolta married the mesenchymal cell's charitable tendencies with an htt-killer. On their own, mesenchymal cells secrete neural growth factors that can restore synaptic connections, though they cannot touch the htt, which continues to plunder. But animal studies showed that strands of RNA can be tailored to chop the htt RNA, decreasing Huntington's symptoms and prolonging survival. Nolta's team of researchers engineered mesenchymal stem cells to manufacture short interfering RNA, or siRNA. Videos of mesenchymal cells engineered to make this siRNA show cells pouring the siRNA into any sick cells they encounter. Her team has a patent pending on this technology.

The first human studies will use the mesenchymal cells without siRNA, to study the effect of the neural growth factors that mesenchymal stem cells produce. The next study will add the siRNA to the mesenchymal cells.

"I'm excited we've now shown that the technology CIRM funded is working, and that mesenchymal stem cells are safe to implant into the brain," Nolta said. "There are so many people in the Huntington's community whom we care about deeply, and we are hoping to have a real impact in treating this disease."

### WHAT IS IT LIKE TO LIVE WITH HUNTINGTON'S DISEASE?

Sherry lives balanced on the odds of a coin toss. • Since she was 9, when her father was diagnosed with Huntington's disease, she's known that she has a 50-50 chance of receiving the same diagnosis. During the next 11 years, as she watched her father fail tragically, his personality changing, his body growing weaker, she coped by staying busy, swimming and playing water polo.

Just knowing she might develop Huntington's is a burden. So many things worry her. "If I trip or fall or mess up at work, I think, 'Oh, I might have HD.' If I'm moody or something, I wonder, 'Is this like the first sign?'"

That's one reason the 27-year-old hasn't taken the genetic test to learn her status. "If I tested positive, I would symptom search even more than I do now."

Another complication: She doesn't give her last name because she fears the discrimination that could follow if her risk status were revealed.

She worries even more about losing the abilities that matter to her. "I love outdoor activities. I love traveling, reading, talking, walking, eating—I'm very good at eating. I just don't want to give up those things I love most in life: my relationships, my independence."

Still she is optimistic about stem cell research. "Whenever I'm having a rough day, I think about it. It just gives me hope."

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